Prevalence of glucocorticoid induced osteonecrosis in the mouse is not affected by treatments that maintain bone vascularity.

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Public Summary:
Objective: Determine if LLP2A-Ale or PTH (1-34) affects the prevalence of glucocorticoid-induced osteonecrosis (ON) in a mouse model. Methods: Eight-week-old young adult male BALB/cJ mice were weight-randomized into Control (Con), glucocorticoid (GC)-only, or concurrent treatments with GC and LLP2A-Ale (250mug/kg or 500mug/kg, IV, Days 1, 14, 28) or parathyroid hormone hPTH (1-34) (40mug/kg, 5x/week). Mice were necropsied after 45days for qualitative evaluation of prevalent ON and quantitative evaluation of vascularity in the distal femoral epiphysis (DFE); and quantitative evaluation of bone mass, microarchitecture, and strength in the distal femoral metaphysis and lumbar vertebral body. Results: The prevalence of ON was 14% in the Con group and 36% in the GC-only group (P=0.07). The prevalence of ON did not differ among GC-only, GC+LLP2A-Ale, and GC+PTH groups. GC-only mice had significantly lower trabecular and cortical bone strength than Con, while GC+LLP2A-Ale (500mug/kg) and GC+PTH (1-34) groups had significantly greater trabecular bone strength than the GC-only group. GC+LLP2A-Ale (250mug/kg and 500mug/kg) and GC+PTH had significantly higher trabecular bone volume than GC-only mice at the vertebrae, distal femoral epiphyses and distal femoral metaphyses. DFE vascularity was lower in GC-only mice than in all other groups. Conclusion: Neither LLP2A-Ale nor hPTH (1-34) reduced the prevalence of GC-induced ON, compared to GC-only mice. However, GC-treated mice given LLP2A-Ale or hPTH (1-34) had better bone mass, microarchitecture, and strength in trabecular-rich regions, and higher levels of vascularity than GC-only mice.

Scientific Abstract:
Objective: Determine if LLP2A-Ale or PTH (1-34) affects the prevalence of glucocorticoid-induced osteonecrosis (ON) in a mouse model. Methods: Eight-week-old young adult male BALB/cJ mice were weight-randomized into Control (Con), glucocorticoid (GC)-only, or concurrent treatments with GC and LLP2A-Ale (250mug/kg or 500mug/kg, IV, Days 1, 14, 28) or parathyroid hormone hPTH (1-34) (40mug/kg, 5x/week). Mice were necropsied after 45days for qualitative evaluation of prevalent ON and quantitative evaluation of vascularity in the distal femoral epiphysis (DFE); and quantitative evaluation of bone mass, microarchitecture, and strength in the distal femoral metaphysis and lumbar vertebral body. Results: The prevalence of ON was 14% in the Con group and 36% in the GC-only group (P=0.07). The prevalence of ON did not differ among GC-only, GC+LLP2A-Ale, and GC+PTH groups. GC-only mice had significantly lower trabecular and cortical bone strength than Con, while GC+LLP2A-Ale (500mug/kg) and GC+PTH (1-34) groups had significantly greater trabecular bone strength than the GC-only group. GC+LLP2A-Ale (250mug/kg and 500mug/kg) and GC+PTH had significantly higher trabecular bone volume than GC-only mice at the vertebrae, distal femoral epiphyses and distal femoral metaphyses. DFE vascularity was lower in GC-only mice than in all other groups. Conclusion: Neither LLP2A-Ale nor hPTH (1-34) reduced the prevalence of GC-induced ON, compared to GC-only mice. However, GC-treated mice given LLP2A-Ale or hPTH (1-34) had better bone mass, microarchitecture, and strength in trabecular-rich regions, and higher levels of vascularity than GC-only mice.